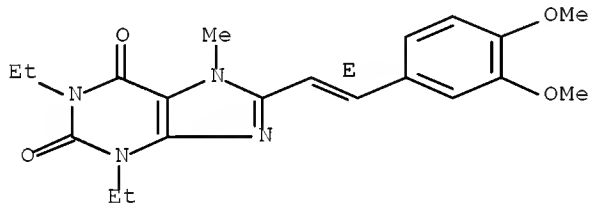
L1 1 S E3

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 155270-99-8 REGISTRY
ED Entered STN: 24 May 1994
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-
3,7-dihydro-7-methyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-
dihydro-7-methyl-, (E)-
OTHER NAMES:
CN Istradefylline
CN KW 6002
FS STEREOSEARCH
MF C20 H24 N4 O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,
CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH,
IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE,
TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



SET EXPAND CONTINUOUSLY CONTINUOUS

FILE 'HCAPLUS' ENTERED AT 10:01:41 ON 07 OCT 2009
L2 106 S L1
L3 2 S L2 AND LEARNING/IT
L4 1 S L3 AND (PY<2004 OR AY<2004 OR PRY<2004)

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Xanthine derivatives and salts and compositions for preventing and/or
treating higher brain dysfunction
ACCESSION NUMBER: 2005:547543 HCAPLUS Full-text
DOCUMENT NUMBER: 143:53542
TITLE: Xanthine derivatives and salts and

compositions for
preventing and/or treating higher brain
dysfunction
INVENTOR(S): Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki,
Shizuo;
Kobayashi, Minoru; Toki, Shinichiro; Seno,
Naoki;
Ikeda, Ken
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056016	A1	20050623	WO 2004-JP18765	20041209 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296137	A1	20050623	AU 2004-296137	20041209 <--
CA 2550130	A1	20050623	CA 2004-2550130	20041209 <--
EP 1709966	A1	20061011	EP 2004-807124	20041209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1889959	A	20070103	CN 2004-80036267	20041209 <--
BR 2004017241	A	20070306	BR 2004-17241	20041209 <--
US 20070078148	A1	20070405	US 2006-579829	20060517 <--

MX 2006005965 A 20060809 MX 2006-5965
20060525 <--
KR 2006124615 A 20061205 KR 2006-711123
20060607 <--
IN 2006CN02490 A 20070608 IN 2006-CN2490
20060706 <--
PRIORITY APPLN. INFO.: JP 2003-410432 A
20031209 <--
WO 2004-JP18765 W
20041209

L5 2 S L2 AND MEMORY/IT
L6 1 S L5 AND (PY<2004 OR AY<2004 OR PRY<2004)
L7 0 S L6 NOT L4
L8 4 S L2 AND (AMNESIA OR ADHD OR LEARNING OR COGNIT?)
L9 1 S L8 AND (PY<2004 OR AY<2004 OR PRY<2004)
L10 0 S L9 NOT L4
L11 9 S L2 AND (ADHD OR ALZHEIMER? OR NEURODEGENERAT?)
L12 1 S L11 AND (PY<2004 OR AY<2004 OR PRY<2004)
L13 1 S L12 NOT L4

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Neuroprotection by caffeine and A2A adenosine receptor inactivation in a
model of Parkinson's disease
AB Recent epidemiol. studies have established an association between the common consumption of coffee or other caffeinated beverages and a reduced risk of developing Parkinson's disease (PD). To explore the possibility that caffeine helps prevent the dopaminergic deficits characteristic of PD, we investigated the effects of caffeine and the adenosine receptor subtypes through which it may act in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) neurotoxin model of PD. Caffeine, at doses comparable to those of typical human exposure, attenuated MPTP-induced loss of striatal dopamine and dopamine transporter binding sites. The effects of caffeine were mimicked by several A2A antagonists (7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo[1,5- c]pyrimidine (SCH 58261), 3,7-dimethyl-1-propargyl xanthine, and (E)-1,3-diethyl-8 (KW-6002)-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H- purine-2,6-dione) (KW-6002) and by genetic inactivation of the A2A receptor, but not by A1 receptor blockade with 8-cyclopentyl-1,3-dipropylxanthine, suggesting that caffeine attenuates MPTP toxicity by A2A receptor blockade. These data establish a potential neural basis for the inverse association of caffeine with the development of PD, and they enhance the potential of A2A antagonists as a novel treatment for this neurodegenerative disease.
ACCESSION NUMBER: 2001:910700 HCAPLUS Full-text
DOCUMENT NUMBER: 136:31603
TITLE: Neuroprotection by caffeine and A2A adenosine receptor
inactivation in a model of Parkinson's disease
AUTHOR(S): Chen, Jiang-Fan; Xu, Kui; Petzer, Jacobus P.; Staal,
Roland; Xu, Yue-Hang; Beilstein, Mark; Sonsalla,

Patricia K.; Castagnoli, Kay; Castagnoli, Neal, Jr.;
Schwarzschild, Michael A.
CORPORATE SOURCE: Molecular Neurobiology Laboratory, Department of
Neurology, Massachusetts General Hospital, Charlestown, MA, 02129, USA
SOURCE: Journal of Neuroscience (2001), 21(10), RC143/1-RC143/6
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
CC 1-11 (Pharmacology)
IT 14114-46-6, 3,7-Dimethyl-1-propargyl xanthine 102146-07-6, 8-Cyclopentyl-1,3-dipropylxanthine 155270-99-8, KW-6002 160098-96-4, SCH 58261
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of caffeine and adenosine antagonists in model of Parkinson's disease)

L14 0 S L2 AND BRAIN ISCHEMIA/IT
L15 1 S L2 AND ISCHEMIA/IT
L16 1 S L15 NOT L4
L17 26 S L2 AND BRAIN/IT
L18 10 S L17 AND (PY<2004 OR AY<2004 OR PRY<2004)

L18 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction
AB A preventive and/or therapeutic agent for higher brain dysfunctions which contains as an active ingredient a xanthine derivative represented, for example, by the following formula (I) or a pharmacol. acceptable salt thereof: (I) (II) wherein R1, R2, and R3 are the same or different and each represents hydrogen, lower alkyl, lower alkenyl, or lower alkynyl; R4 represents cycloalkyl, -(CH2)n-R5, or the formula (II) given above; and X1 and X2 are the same or different and each represents oxygen or sulfur. The higher brain dysfunction includes aging brain damage, brain trauma, cerebrovascular disease, memory disorder, thinking disorder, recognition disorder, behavior disorder, learning disorder, etc.
ACCESSION NUMBER: 2005:547543 HCAPLUS Full-text
DOCUMENT NUMBER: 143:53542
TITLE: Xanthine derivatives and salts and compositions for preventing and/or treating higher brain dysfunction
INVENTOR(S): Kase, Hiroshi; Nakagawa, Yutaka; Shiozaki, Shizuo; Kobayashi, Minoru; Toki, Shinichiro; Seno, Naoki; Ikeda, Ken
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056016	A1	20050623	WO 2004-JP18765	20041209 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296137	A1	20050623	AU 2004-296137	20041209 <--
CA 2550130	A1	20050623	CA 2004-2550130	20041209 <--
EP 1709966	A1	20061011	EP 2004-807124	20041209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1889959	A	20070103	CN 2004-80036267	20041209 <--
BR 2004017241	A	20070306	BR 2004-17241	20041209 <--
US 20070078148	A1	20070405	US 2006-579829	20060517 <--
MX 2006005965	A	20060809	MX 2006-5965	20060525 <--
KR 2006124615	A	20061205	KR 2006-711123	20060607 <--
IN 2006CN02490	A	20070608	IN 2006-CN2490	20060706 <--
PRIORITY APPLN. INFO.:			JP 2003-410432	A 20031209

L18 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine
for treating behavioral disorders
AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also be used for Tic/Tourette's disorder.

ACCESSION NUMBER: 2004:566535 HCAPLUS Full-text
DOCUMENT NUMBER: 141:99728
TITLE: A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine for treating behavioral disorders
INVENTOR(S): Shiozaki, Shizuo; Shimada, Junichi; Kase, Hiroshi; Shindo, Mayumi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	20031224 <--
WO 2004058139	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511779	A1	20040715	CA 2003-2511779	20031224 <--
AU 2003299432	A1	20040722	AU 2003-299432	20031224 <--
EP 1581163	A2	20051005	EP 2003-799729	

20031224 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003017772 A 20051122 BR 2003-17772
20031224 <--
CN 1732005 A 20060208 CN 2003-80107517
20031224 <--
JP 2006513207 T 20060420 JP 2004-563530
20031224 <--
ZA 2005004955 A 20060426 ZA 2005-4955
20050617 <--
MX 2005006860 A 20050818 MX 2005-6860
20050622 <--
US 20060069107 A1 20060330 US 2005-539574
20050728 <--
US 20090023755 A1 20090122 US 2008-239955
20080929 <--
PRIORITY APPLN. INFO.: US 2002-509039P P
20021227 <--
WO 2003-IB6455 W
20031224 <--
US 2005-539574 A1
20050728
IC ICM A61K
CC 1-11 (Pharmacology)
IT Brain, disease
(Gilles de la Tourette syndrome, tic/Tourette's disorder; xanthine
derivative for treatment of behavioral disorders)
IT 155270-99-8
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Translating A2A antagonist KW6002 from animal models to parkinsonian
patients
AB A review. Improving the translation of novel findings from basic laboratory research to better therapies for neurol. disease constitutes a major challenge for the neurosciences. This brief review of aspects of the development of an adenosine A2A antagonist for use in the management of Parkinson's disease (PD) illustrates approaches to some of the relevant issues. Adenosine A2A receptors, highly expressed on striatal medium spiny neurons, signal via kinases whose aberrant activation has been linked to the appearance of parkinsonian signs after dopaminergic denervation and to the motor response complications produced by

dopaminomimetic therapy. To assess the ability of A2A receptor blockade to normalize certain of these kinases and thus benefit motor dysfunction, the palliative and prophylactic effects of the selective antagonist KW6002 were first evaluated in rodent and primate models. In hemiparkinsonian rats, KW6002 reversed the intermittent L-dopa treatment-induced, protein kinase A-mediated hyperphosphorylation of striatal α-amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid receptor GluR1 S845 residues and the concomitant shortening in motor response duration. In 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned monkeys, coadministration of KW6002 with daily apomorphine injections acted prophylactically to prevent dyskinesia onset. These and related preclin. observations guided the design of a limited, randomized, controlled, proof-of-concept study of the A2A antagonist in patients with moderately advanced PD. Although KW6002 alone or in combination with a steady-state IV infusion of optimal-dose L-dopa had no effect on parkinsonian severity, the drug potentiated the antiparkinsonian response to low-dose L-dopa with fewer dyskinesias than produced by optimal-dose L-dopa alone. KW6002 also safely prolonged the efficacy half-time of L-dopa. The results suggest that drugs capable of selectively blocking adenosine A2A receptors could confer therapeutic benefit to L-dopa-treated parkinsonian patients and warrant further evaluation in phase II studies. They also illustrate a strategy for successfully bridging a novel approach to PD therapy from an evolving research concept to pivotal clin. trials.

ACCESSION NUMBER: 2003:904677 HCAPLUS Full-text
DOCUMENT NUMBER: 141:16533
TITLE: Translating A2A antagonist KW6002 from animal models
to parkinsonian patients
AUTHOR(S): Chase, T. N.; Bibbiani, F.; Bara-Jimenez, W.; Dimitrova, T.; Oh-Lee, J. D.
CORPORATE SOURCE: National Institute of Neurological Disorders and
Stroke, Experimental Therapeutics Branch, National
Institutes of Health, Bethesda, MD, 20892-1406, USA
SOURCE: Neurology (2003), 61(11, Suppl. 6), S107-S111
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
CC 1-0 (Pharmacology)
IT Brain
(corpus striatum; translating A2A antagonist KW6002 from animal models
to parkinsonian patients)
IT 155270-99-8, KW6002
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(translating A2A antagonist KW6002 from animal models to parkinsonian
patients)

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L19         7657 S BRAIN ISCHEMIA/IT
L20        19497 S LEARNING/IT
L21          169 S L19 AND L20
L22           24 S L21 AND (PY<2004 OR AY<2004 OR PRY<2004)

L22  ANSWER 12 OF 24  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Cerebral oligemic hypoxia and forebrain ischemia. Common and
different
     long-lasting consequences
AB   The acute and chronic effects of transient cerebral hypoxia,
     produced by bilateral clamping of the carotid arteries (BCCA),
     were compared with those of neuronal necrosis after forebrain
     ischemia produced by 4-vessel occlusion (4-VO) on cognitive
     abilities of rats.  Spatial learning and memory impairments were
     seen in both groups of rats.  In BCCA, long-lasting reference
     memory impairment with no deficiencies in working memory were
     observed up to several months after 60 min BCAA.  Long-lasting
     working memory deficiencies with reference memory impairments
     which showed consolidation over weeks of daily training were seen
     in 4-VO rats.  The brain GABAergic system activity was affected
     differently in the two groups.
ACCESSION NUMBER:         1993:469592  HCAPLUS  Full-text
DOCUMENT NUMBER:          119:69592
ORIGINAL REFERENCE NO.:   119:12537a,12540a
TITLE:                    Cerebral oligemic hypoxia and forebrain
ischemia.
                          Common and different long-lasting consequences
AUTHOR(S):                Sontag, K. H.; Heim, C.; Block, F.; Sieklucka,
M.;
                          Schmidt-Kastner, R.; Melzacka, M.; Osborne,
N.; Laeer,
                          S.; Huether, G.; et al.
CORPORATE SOURCE:         Max-Planck-Inst. Exp. Med., Goettingen, D-
3400,
                          Germany
SOURCE:                   Pharmacol. Cereb. Ischemia 1992, [Int. Symp.],
4th (
                          1992), 471-9.  Editor(s): Krieglstein, Josef;
                          Oberpichler-Schwenk, Heike.  Wiss.
Verlagsges.:
                          Stuttgart, Germany.
                          CODEN: 59ANAV
DOCUMENT TYPE:            Conference
LANGUAGE:                 English
CC   14-10 (Mammalian Pathological Biochemistry)
     Section cross-reference(s): 2
IT   Brain
        (GABAergic system, hypoxia and brain ischemia
        effects on, memory impairment in relation to)
IT   Memory, biological
        (disorder, in hypoxia and brain ischemia)
IT   Learning
        (spatial, disorder, in hypoxia and brain ischemia)
OS.CITING REF COUNT:      7     THERE ARE 7 CAPLUS RECORDS THAT CITE
THIS RECORD
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(7 CITINGS)

L22 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Transient occlusion of carotid arteries leads to disturbed spatial learning and memory in the rat
AB The results of this study demonstrate that transient occlusion of both carotid arteries (BCAA) may cause long-lasting disturbances as exemplified by learning and memory deficits. These results were neither accompanied by cell necrosis nor due to motor deficits. A significant decrease in acetylcholine content in the hippocampus was found 7 and 12 days after 60 min of BCAA.
ACCESSION NUMBER: 1993:231531 HCAPLUS Full-text
DOCUMENT NUMBER: 118:231531
ORIGINAL REFERENCE NO.: 118:40035a,40038a
TITLE: Transient occlusion of carotid arteries leads to disturbed spatial learning and memory in the rat
AUTHOR(S): Heim, Christine; Sieklucka, Maria; Block, Frank; Schmidt-Kastner, Rainald; Jaspers, Robertus; Sontag, Karl heinz
CORPORATE SOURCE: Max-Planck-Inst. Exp. Med., Goettingen, D-3400, Germany
SOURCE: Pharmacol. Cereb. Ischemia (1990), 53-61. Editor(s): Krieglstein, Josef; Oberpichler, Heike. Wiss. Verlagsges.: Stuttgart, Germany. CODEN: 58DIAO
DOCUMENT TYPE: Conference
LANGUAGE: English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
IT Memory, biological
(disorder, after brain ischemia from transient bilateral carotid artery occlusion, acetylcholine of hippocampus in relation to)
IT Brain, composition
(hippocampus, acetylcholine of, brain ischemia from transient bilateral carotid artery occlusion effect on, spatial learning and memory deficits in relation to)
IT Brain, disease
(ischemia, from transient bilateral carotid artery occlusion, spatial learning and memory deficits after, acetylcholine of hippocampus in relation to)
IT Learning
(spatial, disorder, after brain ischemia from transient bilateral carotid artery occlusion, acetylcholine of hippocampus in relation to)
IT 51-84-3, Acetylcholine, biological studies
RL: BIOL (Biological study)
(of hippocampus, brain ischemia from transient bilateral carotid artery occlusion effect on, spatial learning

and memory deficits in relation to)
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)

L22 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Cerebral ischemia model with conscious mice. Involvement of NMDA receptor
activation and derangement of learning and memory ability
AB During anesthesia in mice, both common carotid arteries were occluded. The mortality as well as impairment of brain metabolism depended on the length of cerebral ischemia. Cortical EEG clearly reflected the regional ischemia as evidenced by elec. quiescence. Lower mortality was observed in ischemic mice treated with dextrorphan (30 mg/kg orally). On day 1 (24 h after ischemia), there were impairments in complex motor coordination, multichoice swim performance, and step-through or thermal pain-motivated avoidance responses. Thereafter the performance progressively improved. The improvement depended on the period of resumption of cerebral blood flow. Redns. in the degree of habituation and exploratory activity were also clearly observed following an ischemic insult. Dextrorphan (1-30 mg/kg i.p.) given to ischemic mice was effective in the habituation and step-through-type passive avoidance test paradigms. The decline in cognition as observed with ischemic mice was due to the temporal and reversible derangement of the neuronal network. Excessive released glutamate was probably of major pathogenic importance in the consequences of cerebral ischemia based on the pos. effects of the N-methyl-D-aspartate (NMDA) receptor agonist dextrophan. The simple technique could be useful in elucidating the pathophysiol. mechanisms of ischemic derangement of the cerebral organization. The model could also be used to assess the efficiency of drugs with high clin. predictive value.
ACCESSION NUMBER: 1990:569734 HCAPLUS Full-text
DOCUMENT NUMBER: 113:169734
ORIGINAL REFERENCE NO.: 113:28775a,28778a
TITLE: Cerebral ischemia model with conscious mice. Involvement of NMDA receptor activation and derangement of learning and memory ability
AUTHOR(S): Himori, Norio; Watanabe, Hiroshi; Akaike, Nobuhide;
Kurasawa, Mitsue; Itoh, Jiro; Tanaka, Yushiro
CORPORATE SOURCE: Dep. Pharmacol., Nippon Roche Res. Cent., Kamakura,
247, Japan
SOURCE: Journal of Pharmacological Methods (1990), 23(4), 311-27
CODEN: JPMED9; ISSN: 0160-5402
DOCUMENT TYPE: Journal
LANGUAGE: English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
IT Behavior
Learning
Memory, biological
(Brain ischemia and dextrorphan effects on, methylaspartate receptors in)

IT Receptors
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(for methylaspartate, in brain ischemia, behavioral changes in relation to)
IT 125-73-5, Dextrorphan
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(brain ischemia response to, methylaspartate receptors in, behavioral effects in relation to)
OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS
RECORD (17 CITINGS)

L22 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Postischemic insulin reduces spatial learning deficit following transient
forebrain ischemia in rats
AB The ability of postischemic insulin administration to modify the structural and neurobehavioral consequences of cerebral ischemia in rats was investigated. Forebrain ischemia was induced in fed rats by combining controlled systemic hypotension with bilateral carotid artery clamping for 10.5 min. Following clamp release, 1 group of rats was given insulin (2 IU/kg, s.c., b.i.d.) for 1 wk. An ischemic-control group of rats received no postischemic treatment. A sham-ischemia group of rats was used as a behavioral control. Throughout the recovery period until sacrifice, the drinking water of all rats was supplemented with 25% glucose. Rats were trained on 2 water maze place navigation tasks 1-2 mo after ischemia. Escape latencies and swim patterns were recorded. Performance in the insulin-treated group was better than that in the ischemia-control group on both tasks and did not differ from that of the sham-ischemia group. Improvement in behavior correlated with a reduction in CA1 hippocampal necrosis in the insulin-treated group. Apparently postischemic treatment with insulin improves neurobehavioral performance in addition to lessening ischemia neuronal necrosis.
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